REMARKS

Amendments to the Specification:

Page 24, lines 28 and 30; page 35, line 12; page 36, line 14; page 37, line 18; and page 39, line 3 have been amended to refer to the appropriate sequence number listed in the Sequence Listing.

The drawings on page 37 have been removed from the specification and included in a new drawing sheet attached hereto as FIGS. 4a, 4b, and 4c. The paragraph starting at page 37, line 3 of the application as filed has been amended to refer to FIGS. 4a, 4b, and 4c. An appropriate brief description of the new figures has been added at the bottom of page 11.

Paragraphs starting at page 4, line 6; page 14, line 9; page 16, line 16; page 17, line 27; page 33, lines 5, 22, and 28; page 34, line 30; page 36, line 14; page 37, line 13; and page 39, line 21 have been amended to remove typographical errors.

No new matter has been added.

Amendments to the Claims:

Claim 1 has been amended to remove reference to elements conjugated to a binding site for a sequence-specific regulatory factor and now recites elements covalently bonded thereto, as originally claimed in Claim 4. Support for the claim as amended can therefore be found in Claim 4 as originally filed.

Claim 4 has been canceled herein without prejudice on the merits. Claims 5, 11, 12, 14, 20, 21, 23, 29, 30, 33, and 37 were previously canceled.

Claims 16, 17, 25, and 26 have been amended to remove duplication of the word "step."

Claim 1, 13, 22, and 34 have been amended to correct the spelling of "excluding."

Claims 35, 36, and 38 have been amended to correct punctuation.

Claims 10, 19, 28, 32, and 36 have been amended to define "aptamer" as "comprising a double-stranded DNA or single-stranded RNA moiety that binds to a specific molecular target." Support for the claim as amended can be found in the specification on page 12, lines 13-15.

Claim 22 has been amended to remove reference to "binding of natural transcription factors" and now recites that "the test compound is known to modulate transcription of a gene operationally linked with the sequence-specific transcription factor binding site defined in the

nucleic acid target." Support for the claim as amended can be found in the specification on page 6, lines 1-7 and page 13, lines 15-18.

Claims 31 and 34 have been amended to remove recitation of a "desired" binding site for a sequence-specific regulatory factor and now recite that the isolated nucleic acid target "defines one and only one putative binding site for a sequence-specific regulatory factor." Support for the claims as amended can be found in the specification on page 7, lines 6-8.

Claims 1-3, 6-10, 13, 15-19, 22, 24-28, 31, 32, 34-36, and 38 are pending.

Favorable consideration of the claims is respectfully requested.

Rejection of Claims 10, 19, 28, 32, and 36 over U.S.C. §112, Second Paragraph:

Applicant submits that this rejection has been overcome by amendment of the claims.

The Office has rejected Claims 10, 19, 28, 32, and 36 as indefinite for failing to indicate a structural difference between a "linker moiety" and an "aptamer." Claims 10, 19, 28, 32, and 36 have been amended to define "aptamer" as "comprising a double-stranded DNA or single-stranded RNA moiety that binds to a specific molecular target." Applicant submits that the current claims now positively recite a structural difference between a "linker moiety" and an "aptamer."

Claims 22 and 24-28 have been rejected as indefinite because the Office has contended that it is unclear what is accomplished by performing the claimed method steps. The Office specifically notes that step (a) part (iii) requires the test compound in the assay to be "known to modulate binding of natural transcription factors to the transcription factor binding site defined in the nucleic acid target." Claims 24-28 depend from Claim 22. Claim 22 has been amended herein to remove reference to "binding of natural transcription factors" and now recites that "the test compound is known to modulate transcription of a gene operationally linked with the sequence-specific transcription factor binding site defined in the nucleic acid target." Applicant submits that, as amended, Claim 22 and dependent Claims 24-28 are now clear regarding what is accomplished by performing the claimed method steps, specifically: the recited steps determine whether the test compound alters binding of a sequence-specific transcription factor to the nucleic acid target.

Withdrawal of this rejection is respectfully requested.

Rejection of Claims 1-3, 6-10, 31, 32, 34-36, and 38 over U.S.C. §102(e) over Stanojevic (U.S. Patent Publication No. 2003/105045):

As applied to Claims 1-3 and 6-10, this rejection has been overcome by incorporating the subject matter of Claim 4 into Claim 1.

Claim 4 (which depended from Claim 1) recited that the anchor moiety is covalently bonded to the nucleic acid target. Claim 4 was not subject to this rejection. Because Claim 1 has been amended to incorporate the subject matter of Claim 4. Applicant submits that Claim 1 and all claims dependent therefrom, including Claims 2, 3, and 6-10 are free of this rejection.

In light of the amended claims, withdrawal of this rejection with respect to Claims 1-3 and 6-10 is respectfully requested.

As applied to Claims 31, 32, 34-36, and 38, this rejection is believed to have been overcome, in part, by amendment to the claims, and is, in part, respectfully traversed.

Claims 31 and 34 have been amended to remove recitation of a "desired" binding site for a sequence-specific regulatory factor and now recites that the isolated nucleic acid target "defines one and only one putative binding site for a sequence-specific regulatory factor." Therefore, the compositions and kits recited in Claims 31, 32, and 34-36 now all require that the nucleic acid target define one and only one putative binding site (Claims 31, 32, and 34) or actual binding site (Claims 35, 36, and 38) for a sequence-specific regulatory factor. Note that according to the Merriam-Webster Online Dictionary, "putative" is defined as "commonly accepted or supposed" or "assumed to exist or to have existed." See Exhibit A, attached hereto. Applicants therefore submit that there is nothing ambiguous about the word "putative."

In contrast, the single-stranded DNA taught by Stanojevic in Table 1 and paragraphs [0042], [0045], and [0066], as cited by the Office, do not define an actual or even a putative binding site for a sequence-specific regulatory factor. Stanojevic characterizes the single-stranded DNA oligonucleotides in the above-mentioned sections exclusively as DNA-binding domains. In paragraph [0042], Stanojevic states that the oligonucleotides "are thought to bind in the major groove of the DNA helix." Paragraph [0045] of Stanojevic is directed to the DNA-binding properties of peptide nucleic acids (PNAs). Stanojevic here specifically states, "Peptide nucleic acids can bind to single-stranded DNA by Watson-Crick base pairing and can form triple helices to DNA/PNA duplexes..." Stanojevic further states in this section that the discussed properties

of PNA "make PNA a very attractive choice for an ATF **DNA-binding domain**" (emphasis added). Paragraph [0066] of Stanojevic discusses the DNA-binding of an oligonucleotide presented in Table 1, SEQ ID NO: 5. Stanojevic states that the oligonucleotide "binds the corresponding target double-stranded [DNA] sequence by forming a triple-helical complex at physiological pH." Thus, all the passages referenced by the Office as supporting a binding site for a sequence-specific regulatory factor **only** mention DNA-binding properties and are **completely silent** with respect to regulatory factor binding. There is no indication in these passages or elsewhere in Stanojevic that the polynucleotides contain or comprise commonly accepted or supposed binding sites for sequence-specific regulatory factors.

In short, Applicant submits that Stanojevic does not teach, either in the passages referenced by the Office or elsewhere in the reference, an isolated nucleic acid target that defines one and only one sequence-specific regulatory factor binding site, whether actual or putative, which is covalently bonded to an anchor moiety. This combination of elements is positively required by Claims 31, 32, 34-36, and 38. Stanojevic therefore fails to teach all the required elements of the claims. Because Stanojevic fails to teach all the required elements of the claims, Applicant submits that the current rejection over Stanojevic is untenable.

Withdrawal of this rejection with respect to Claims 31, 32, 34-36, and 38 is also therefore respectfully requested.

Rejection of Claims 31, 32, and 34 under U.S.C. §103(a) over Essigmann et al. (U.S. Pat. No. 5,879,917):

Applicant respectfully traverses this rejection.

Applicant submits that Essigmann et al. do not teach all the positively recited requirements of Claims 31, 32, and 34. Notably, Essigmann et al. do not teach an "anchor moiety" as that term is used in the present application. As defined in the claims, an anchor moiety is disposed between a linker containing a test compound and a nucleic acid target. However, the crosslinking agents of Essigmann et al. are disposed between a transcription factor and a transcription factor decoy (contended "nucleic acid target"), not between a linker and a nucleic acid target. The crosslinking agents of Essigmann et al. are thus not structurally analogous to the anchor moiety of the claimed composition. Therefore, Essigmann et al. do not teach an "anchor

moiety" as positively defined in the claims.

Applicant also submits that Essigmann et al. do not teach that the anchor moiety is covalently bonded at a point **proximate** to the binding site for a sequence-specific regulatory factor, as required in Claim 34, or at a point **proximate** to the binding site for a sequence-specific regulatory factor and **not within the binding site**, as required by Claims 31 and 32. "Proximate" is defined in the specification on page 13, lines 12-14 as requiring that "the anchor moiety binds at a distance at least 2 nucleotides distant from either end of the binding site, and less than 500 nucleotides distant from either end of the binding site." By contrast, Essigmann et al. define transcription factor decoys as sites that mimic endogenous genomic binding sites (see column 14, lines 40-42) wherein the transcription factor binds **within the binding site** (see column 14, line 20 through column 21, line 20). Essigmann et al. therefore do not teach binding of an anchor moiety at a point proximate to the binding site.

Applicant further submits that Essigmann et al. do not teach a "test compound conjugated to the linker moiety" as recited in Claims 31 and 34. As defined in the specification at page 26, lines 20-22, "The test compound can be any moiety, without limitation, that is desired to be tested for its ability to modulate binding of regulatory factors to a nucleic acid target." The Office considers the "genotoxic compound" of Essigmann et al. analogous to the currently claimed "test compound." However, the composition taught by Essigmann et al. is not configured to test the role of the genotoxic agent in modulating binding of regulatory factors to a nucleic acid target. Rather, the composition of Essigmann et al. is configured to bind to cellular DNA to form a genomic lesion. Essigmann et al. are completely silent with respect to affecting binding of regulatory factors to the genomic sites or even testing the binding of such regulatory factors. Essigmann et al. therefore do not teach a test compound as recited in Claims 31, 32, and 34.

Finally, to maintain the Office's analogy mentioned above, wherein the crosslinking agent correlates to the anchor moiety (which it must for even a putative teaching of all the claimed requirements to be maintained), the composition taught by Essigmann et al. would necessarily preclude any effects of the genotoxic compound on modulating binding of the transcription factor to the target nucleotide sequence. The crosslinking agent would irreversibly link the transcription factor to the DNA sequence under transcription conditions. Therefore, the entire composition of Essigmann et al. as characterized by the Office would not constitute a "test compound" as

defined by the Applicant.

Applicant therefore submits that this rejection is improper. Withdrawal of this rejection is respectfully requested.

Rejection of Claims 35, 36, and 38 under U.S.C. §103(a) over Essigmann et al. and Ahern (of Record):

Applicant respectfully traverses this rejection.

As with Claims 31, 32, and 34, Claims 35, 36, and 38 require an anchor moiety, wherein the anchor moiety is covalently bound at a point **proximate** to the binding site for a sequence-specific regulatory factor or at a point **proximate** to the binding site for a sequence-specific regulatory factor and **not within the binding site**. For reasons described above, Applicant submits that Essigmann et al. do not teach these requirements.

Applicant agrees with the Office's statement that Essigmann et al. do not teach a kit with a compound "where the genotoxic compound is not covalently attached to the linker" (page 19 of Office Action). However, Applicant traverses that it would have been obvious to one of ordinary skill in the art to modify the teachings of Essigmann et al. to include such a compound. The combination of Essigmann et al. and Ahern fail to provide any reason why using numerous different genotoxic agents that can separately be selected from the agents taught for attachment to the linker would be desired or beneficial. There's simply no motivation provided by the combined references to make such a modification to the actual teaching of the Essigmann et al. reference. The only motivation to make such a change is provided by Applicant's own specification. But the Office is not at liberty to use Applicant's own specification to provide the motivation that is lacking in the applied combination of references.

Applicant submits that this rejection is improper. Withdrawal of this rejection is respectfully requested.

Rejection of Claims 1-4, 6-10, 13, and 15-19 under 35 U.S.C. §103(a) over Essigmann et al. and Hunt et al. :

As with Claims 31 and 32, independent Claims 1 and 13 require an anchor moiety, wherein the anchor moiety is covalently bound at a point **proximate** to the binding site for a

sequence-specific regulatory factor and **not within the binding site**. Claims 1 and 13 further require a test compound bonded to the linker moiety. For reasons described above, Applicant submits that Essigmann et al. do not teach these requirements. Applicants further submit that Hunt et al. do not teach these requirements.

Finally, Essigmann teaches that the crosslinking agent covalently binds a linker to a transcription factor. If the Office were to maintain the analogy wherein the crosslinking agent correlates to the anchor moiety, which it must for even a putative teaching of the currently claimed method to be maintained, the complex taught by Essigmann would necessarily preclude any effects of the genotoxic compound in modulating binding of the transcription factor to a DNA sequence. The crosslinking agent would irreversibly bind the transcription factor to the DNA sequence under transcription conditions. Therefore, the composition taught by Essigmann would not work as a test compound for the claimed methods.

Applicant submits that this rejection is improper. Withdrawal of this rejection is respectfully requested.

Rejection of Claims 1-3, 6-10 under U.S.C. §103(a) over Ansari et al. (2001, of Record) and Aurora et al. (2002, of Record):

Applicant submits that this rejection has been overcome by amendment of the claims.

Claim 4, which depends from Claim 1 and recites that the anchor moiety is covalently bonded to the nucleic acid target, was not subject to this rejection. Claim 1 has been amended to incorporate the subject matter of Claim 4. Applicant therefore submits that Claim 1 and all claims dependent therefrom, including Claims 2-3 and 6-10 are free of this rejection.

Withdrawal of this rejection is respectfully requested.

CONCLUSION

In light of the above amendments and accompanying remarks, Applicant submits that the application is now in condition for allowance. Early notification of such action is earnestly solicited. If any questions arise, please contact the undersigned attorney. Telephone calls related to this application are welcomed and encouraged. The Commissioner is authorized to charge any fees or credit any overpayments relating to this application to deposit account number 18-2055.

Respectfully Submitted,

Joseph T. Leone, Reg. No. 37,170
CUSTOMER NO.: 60961
DEWITT ROSS & STEVENS S.C.
2 East Mifflin Street, Suite 600
Madison, WI 53703-2865
Telephone: (608) 255-8891
Facsimile: (608) 252-9243

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FIG. 4a

a)

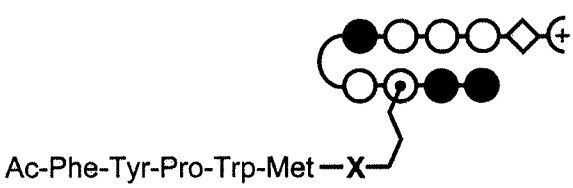


FIG. 4b

b)

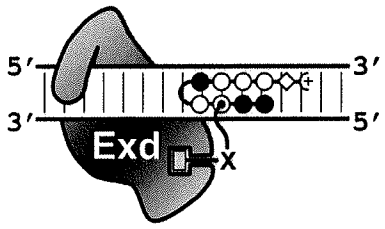
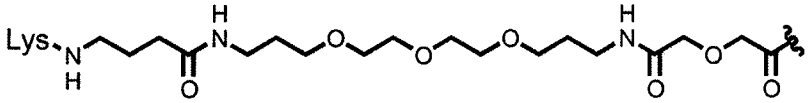
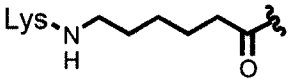
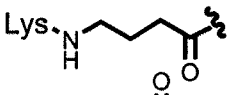


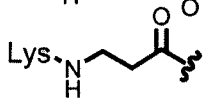
FIG. 4c

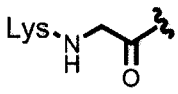
c)

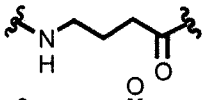
1: X= 

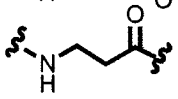
2: X= 

3: X= 

4: X= 

5: X= 

6: X= 

7: X= 

8: X= Lys

Exhibit A

putative

One entry found.

On Off

Main Entry: **pu·ta·tive**
Pronunciation: \'pyü-tə-tiv\
Function: *adjective*
Etymology: Middle English, from Late Latin *putativus,* from Latin *putatus,* past participle of *putare* to think
Date: 15th century

1 : commonly accepted or supposed
2 : assumed to exist or to have existed
— pu·ta·tive·ly *adverb*

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